α'

transforming growth factor β1 (Munger et al., Cell (Cambridge, Mass) 96:319-328, 1999), and in viral infections (Virology 239:71-77, 1997).

In the Claims:

Please DELETE Claim

Please AMEND Claims 1, 4 and 5 as follows:

1. (Amended)

A compound of the formula

 $U-V-A-(Alk)_i-(C(O)-NH)_h-(Alk)_g-B$

or a pharmaceutically acceptable salt thereof, wherein g, h and j are each independently 0 or 1; provided when h is 0, then g is 0;

each Alk is independently a alkyl radical;

5 m

U represents amidino, guanidino, -(G-alkyl)_k-NH-R₁, -(G-alkyl)_k-NH-C(Q)-R₁, -(G-alkyl)_k-C(Q)-N(R)-R₁, -(G-alkyl)_k-NH-C(Q)-O-R₁ or -(G-alkyl)_k-O-C(Q)-N(R)-R₁ radical; or U represents a hydroxyalkyl-G- radical which is optionally substituted by a cycloalkyl, aryl, heteroaryl or heterocyclyl, wherein the cycloalkyl, aryl, heteroaryl and heterocyclyl radicals are optionally substituted by 1-3 radicals of R_2 ;

wherein k is 0 or 1;

G represents a bond, O, S or NH;

Q represents O, S, NH, N-CN or N-alkyl;

R is a radical of hydrogen or alkyl;

R₁ is a radical of alkyl, haloalkyl, R₂₁R₂₂N-alkyl, R₂₁O-alkyl, R₂₁S-alkyl, cycloalkyl, cycloalkyl alkyl, aryl, aryl-alkyl, heteroaryl-alkyl, heterocyclyl or heterocyclyl-alkyl, wherein the

cycloalkyl, aryl, heteroaryl and heterocyclyl radicals are optionally substituted by 1-3 radicals of R₂;

wherein R_{21} and R_{22} are each independently a radical of hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkyl, aryl, aryl-alkyl, heteroaryl-alkyl, heteroaryl-alkyl, heterocyclyl or heterocyclyl-alkyl, wherein the cycloalkyl, aryl, heteroaryl and heterocyclyl radicals are optionally substituted by 1-3 radicals of R_2 ;

each R₂ is independently a halo, alkyl, alkoxy, alkylthio, haloalkyl, haloalkoxy, hydroxy, carboxy, cyano, azido, amidino, guanidino, nitro, amino, alkylamino or dialkylamino radical or two adjacent R₂ radicals on an aryl or heteroaryl radical represent a methylenedioxy, ethylenedioxy or propylenedioxy radical;

V represents a radical of formula

$$W_{2} \longrightarrow W_{5} \longrightarrow W_{6} \longrightarrow W_{6} \longrightarrow W_{6} \longrightarrow W_{6} \longrightarrow W_{6} \longrightarrow W_{4} \longrightarrow W_{3} \longrightarrow W_{4} \longrightarrow W_{3} \longrightarrow W_{4} \longrightarrow W_{3} \longrightarrow W_{4} \longrightarrow W_{3} \longrightarrow W_{4} \longrightarrow W_{5} \longrightarrow W_{5$$

wherein each W_2 , W_3 , W_4 and W_5 is C-R₄; provided the total number of cycloalkyl, aryl, heteroaryl, heterocyclyl, carboxy, -C(O)-O-R₁₉, -C(O)-R₁₉, -C(O)-NH-R₁₉, -C(O)-N(R₁₉)₂ and -R₁₉ radicals in W_2 , W_3 , W_4 and W_5 is 0-2;

each W₆ is C-H; and

each R_4 is independently a hydrogen, halo, alkyl, alkoxy, alkylthio, haloalkyl, haloalkoxy, hydroxy, cyano, carboxy, $-C(O)-O-R_{19}$, $-C(O)-R_{19}$, $-C(O)-NH-R_{19}$, $-C(O)-N(R_{19})_2$, cycloalkyl, cycloalkyl-alkyl, aryl, aryl-alkyl, heteroaryl, heteroaryl-alkyl, heterocyclyl or heterocyclyl-alkyl radical, wherein the cycloalkyl, aryl, heteroaryl and heterocyclyl radicals are optionally substituted by 1-3 radicals of R_2 ; or two adjacent R_4 radicals taken together with the carbon atoms to which they are attached represent a fused-phenyl or fused-heteroaryl of 5-6 ring members, wherein the phenyl and heteroaryl radicals are optionally substituted by 1-3 radicals of R_2 ;

R₅, R₆ and R₇ are each independently a hydrogen, halo, alkyl, alkoxy, alkylthio, haloalkyl, haloalkoxy, hydroxy or cyano radical; or R₅ and R₆ or R₆ and R₇ taken together with the carbon atoms to which they are attached represent a fused-phenyl or fused-heteroaryl of 6 ring members, wherein the phenyl and heteroaryl radicals are optionally substituted by 1-3 radicals of R₂; or R₃ and R₆ taken together with the carbon atoms to which they are attached represent a fused-heteroaryl of 6 ring members optionally substituted by 1-3 radicals of R₂;

A represents a radical of formula

$$R_{8}$$
 R_{9} or R_{10} R_{12}

 R_8 , R_9 , R_{10} , R_{11} and R_{12} are each independently a hydrogen or alkyl radical; or -CR₈R₉-represents a -C(O)-;

B represents a radical of formula

L

5 W

wherein (a) R_{15} is a hydrogen or alkyl radical; and R_{17} is (1) an aryl, heteroaryl, -NH-C(O)- R_{19} , -C(O)-NH- R_{19} , -NH-C(O)-NH- R_{19} , -NH-C(O)-O- R_{19} , -S(O)₂- R_{19} , -NH-S(O)₂- R_{19} , -S(O)₂-NH- R_{19} or -NH-S(O)₂-NH- R_{19} radical, or (2) an alkyl radical substituted by a radical of aryl, heteroaryl, -NH-C(O)- R_{19} , -C(O)-NH- R_{19} , -NH-C(O)-NH- R_{19} , -O-C(O)-NH- R_{19} , -NH-C(O)-O- R_{19} , -S(O)₂- R_{19} , -NH-S(O)₂-R₁₉, -S(O)₂-NH- R_{19} or -NH-S(O)₂-NH- R_{19} ; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of R_2 ; or

(b) R_{17} is a hydrogen or alkyl radical; and R_{15} is (1) an aryl, heteroaryl, cycloalkyl, heterocyclyl, - NH-C(O)-R₁₉, -C(O)-NH-R₁₉, -NH-C(O)-NH-R₁₉, -O-C(O)-NH-R₁₉, -NH-C(O)-O-R₁₉, -S(O)₂-R₁₉, -NH-S(O)₂-R₁₉, -S(O)₂-NH-R₁₉ or -NH-S(O)₂-NH-R₁₉ radical, or (2) an alkyl radical substituted by a radical of aryl, heteroaryl, cycloalkyl, heterocyclyl, -NH-C(O)-R₁₉, -C(O)-NH-R₁₉, -NH-C(O)-NH-R₁₉, -NH-C(O)-O-R₁₉, -S(O)₂-R₁₉, -NH-S(O)₂-R₁₉, -S(O)₂-NH-R₁₉ or -NH-S(O)₂-NH-R₁₉ radical; wherein the cycloalkyl, aryl, heteroaryl and heterocyclyl radicals are optionally substituted by \lambda -3 radicals of R₂;

provided that when a nitrogen atom is attached to the carbon atom to which R_{15} is attached, then R_{15} is (1) an aryl, heteroaryl, cycloalkyl, heterocyclyl or -C(O)-NH-R₁₉ radical, or (2) an alkyl radical substituted by a radical of aryl, heteroaryl, cycloalkyl, heterocyclyl, -NH-C(O)-R₁₉, -C(O)-NH-R₁₉, -NH-C(O)-NH-R₁₉, -NH-C(O)-O-R₁₉, -S(O)₂-R₁₉, -NH-S(O)₂-R₁₉, -S(O)₂-NH-R₁₉ or -NH-S(O)₂-NH-R₁₉;

wherein R₁₉ is a alkyl, cycloalkyl, cycloalkyl-alkyl, aryl, aryl-alkyl, heteroaryl, heteroaryl-alkyl, heteroaryl and heterocyclyl or heterocyclyl-alkyl, wherein the cycloalkyl, aryl, heteroaryl and heterocyclyl radicals are optionally substituted by 1-3 radicals of R₂;

R₁₆ and R₁₈ are each independently a hydrogen or alkyl radioal; and

a x

E is a radical of carboxy, amido, tetrazolyl, $-C(O)-O-R_{20}$, $-C(O)-NH-R_{20}$, $-C(O)-NH-S(O)-R_{20}$, $-C(O)-NH-S(O)-R_{20}$;

50b 131

wherein R_{20} is an alkyl, cycloalkyl, aryl, heteroaryl or heterocyclyl radical or an alkyl radical substituted by 1-3 radicals of halo, hydroxy, carboxy, amino, cycloalkyl, aryl, heteroaryl or heterocyclyl, wherein the cycloalkyl, aryl, heteroaryl and heterocyclyl radicals are optionally substituted by 1-3 radicals of R_2 ; and

provided that when U represents amidino, guanidino, -C(Q)-NH-R₁ or -NH-C(Q)-NH-R₁ radical, wherein Q represents NH, N-CN or N-alkyl, then at least one of g, h or j is 1.

a3

4. (Amended) The compound of Claim 2 or a pharmaceutically acceptable salt thereof, wherein

each Alk is independently a C1-C6 alkyl radical;

V represents a radical of formula

$$W_3$$
 W_4 W_5 W_4 W_3 W_3 ; and

 R_8 , R_9 , R_{10} , R_{11} and R_{12} are each independently a hydrogen or methyl radical; or -CR₈R₉-represents a -C(O)-.

5 N

5. (Amended) The compound of Claim 4 or a pharmaceutically acceptable salt thereof, wherein

each Alk is independently a C₁-C₄ alky radical;

 a^3

U represents amidino, guanidino, -(G-(C₁-C₈ alkyl))_k-NH-R₁, -(G-(C₁-C₈ alkyl))_k-NH-C(Q)-R₁, -(G-(C₁-C₈ alkyl))_k-C(Q)-N(R)-R₁, -(G-(C₁-C₈ alkyl))_k-NH-C(Q)-N(R)-R₁ or -(G-(C₁-C₈ alkyl))_k-NH-C(Q)-Q-R₁ radical;

G represents a bond, O or NH;

Sub 133 Q represents O, S, NH, N-CN or N-(C₁-C₄ alkyl);

R is a radical of hydrogen or C₁-C₄ alkyl;

 R_1 is a radical of C_1 - C_6 alkyl, halo(C_1 - C_6 alkyl) of 1-5 halo radicals, $R_{21}R_{22}N$ -(C_1 - C_6 alkyl), $R_{21}O$ -(C_1 - C_6 alkyl), C_3 - C_8 cycloalkyl, C_3 - C_8 cycloalkyl(C_1 - C_6 alkyl), aryl, aryl(C_1 - C_6 alkyl), heteroaryl of 5-10 ring members, heteroaryl(C_1 - C_6 alkyl) of 5-10 ring members, heterocyclyl of 5-8 ring members or heterocyclyl(C_1 - C_6 alkyl) of 5-8 ring members, wherein the cycloalkyl, aryl, heteroaryl and heterocyclyl radicals are optionally substituted by 1-3 radicals of R_2 ;

 R_{21} and R_{22} are each independently a radical of hydrogen, C_1 - C_8 alkyl, aryl, aryl(C_1 - C_4 alkyl), heteroaryl of 5-10 ring members or heteroaryl(C_1 - C_4 alkyl) of 5-10 ring members, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of R_2 ;

each R₂ is independently a halo, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ alkylthio, halo(C₁-C₂ alkyl) of 1-5 halo radicals, halo(C₁-C₂ alkoxy) of 1-5 halo radicals, hydroxy, carboxy, cyano, azido, amidino, guanidino, nitro, amino, C₁-C₄ alkylamino or di(C₁-C₄ alkyl)amino radical or two adjacent R₂ radicals on an aryl or heteroaryl radical represent a methylenedioxy, ethylenedioxy or propylenedioxy radical;

each R_4 is independently a hydrogen, halo, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, C_1 - C_4 alkylthio, halo(C_1 - C_2 alkyl) of 1-5 halo radicals, halo(C_1 - C_2 alkoxy) of 1-5 halo radicals, hydroxy, cyano, carboxy, -C(O)- C_1 - C_2 , - C_3 - C_4 cycloalkyl, C_3 - C_6 cycloalkyl, C_3 - C_6 cycloalkyl(C_1 - C_4 alkyl), aryl, aryl(C_1 - C_4 alkyl), heteroaryl of 5-10 ring members, heteroaryl(C_1 - C_4 alkyl) of 5-8 ring members, heterocyclyl of 5-8 ring

PATENT APPLICATION

Q3

members radical, wherein the cycloalkyl, aryl, heteroaryl and heterocyclyl radicals are optionally substituted by 1-3 radicals of R₂; and

5 b

R₂₀ is a C₁-C₄ alkyl, arylor heteroaryl of 5-10 ring members or a C₁-C₄ alkyl radical substituted by 1-3 radicals of halo, hydroxy, carboxy, amino, aryl, heteroaryl of 5-10 ring members or heterocyclyl of 5-8 ring members, wherein the aryl, heteroaryl and heterocyclyl radicals are optionally substituted by 1-3 radicals of R₂.